UNITED STATES DISTRICT COURT
SOUTHERN DISTRICT OF INDIANA
INDIANAPOLIS DIVISION

DEBRA L. TUCKER,	)	
	)	
Plaintiff,	)	
vs.	)	NO. 1:04-cv-01748-DFH-WTL
	)	
SMITHKLINE BEECHAM CORPORATION,	)	
	)	
Defendant.	)	

UNITED STATES DISTRICT COURT
SOUTHERN DISTRICT OF INDIANA
INDIANAPOLIS DIVISION

DEBRA L. TUCKER, individually and as personal representative of the Estate of Rick G. Tucker,	)	
Plaintiff,	)	
v.	)	CASE NO. 1:04-cv-1748-DFH-WTL
SMITHKLINE BEECHAM CORP., d/b/a Glaxosmithkline, a Pennsylvania corporation,	)	
Defendant.	)	

ENTRY ON PLAINTIFF'S MOTION TO RECONSIDER

Defendant SmithKline Beecham Corp. ("GSK") manufactures and sells pharmaceuticals, including Paxil, an antidepressant. Plaintiff Debra Tucker brought this wrongful death suit under Indiana state law against GSK, claiming that her older brother, Father Rick Tucker, committed suicide as a result of taking Paxil. She contends that GSK breached its duty to warn of an increased suicide risk in adults taking Paxil. Finding that the federal Food and Drug Administration ("FDA") required GSK to include language in its drug label that conflicted directly with the warning that Tucker argues was required under Indiana law, this court dismissed Tucker's state law claims as preempted by federal law. See *Tucker v.*

SmithKline Beecham Corp., 2007 WL 2726259 (S. D. Ind. Sept. 19, 2007).[1] Tucker filed a motion under Rule 59 asking the court to reconsider its decision. As explained below, Tucker's motion to reconsider is granted and the judgment is vacated. In finding conflict preemption, the court failed to appreciate the significance of the fact that the FDA regulations allow a manufacturer to modify pharmaceutical labels unilaterally and immediately, without prior FDA approval, when the manufacturer has reasonable evidence of a serious hazard.

General Background and Standard of Review

Conflict preemption arises when it is impossible to comply with both state and federal requirements or when state law stands as an obstacle to the accomplishment and execution of the full purposes and objectives of Congress. *Sprietsma v. Mercury Marine*, 537 U.S. 51, 64 (2002) (internal quotations and citations omitted); *Crosby v. Nat'l Foreign Trade Council*, 530 U.S. 363, 372-73 (2000); *Hillsborough County v. Automated Medical Laboratories, Inc.*, 471 U.S. 707, 713 (1985). GSK argued that Tucker's claims directly conflicted with (1) the FDA-mandated labeling for Paxil; (2) the FDA's "consistent and repeated" determinations, during the period before and after Father Tucker's death in September 2002, that there is no scientific basis for the suicide warning Tucker claims GSK should have included in its labeling for adults; and (3) the FDA's

[1]GSK also moved for summary judgment on Tucker's claims on the issues of causation and breach of duty. The court did not reach those issues in its September 19, 2007 entry but will need to do so now.

statement in May 2006 that it regards the additional warnings advocated by Tucker as "false, misleading, and potentially harmful to the public," and that placement of those warnings on the label for Paxil would render the drug misbranded and unlawful as a result. See GSK Br. (Preemption) at 1-2.

While GSK's motion was under advisement, GSK submitted additional evidence that in May 2007, the FDA required a revised warning label for Paxil addressing the issue of adult suicidality, which the court believed "affirmatively reject[ed] the hypothesis" that there is an association between Paxil and suicide in adults. 2007 WL 2726259, at *9. Accordingly, the court found Tucker's claims to be preempted by federal law. In moving the court to reconsider its ruling, Tucker argues that no conflict exists because the FDA has not, in fact, precluded GSK from including in its current label Paxil-specific warning language, such as that contained in its 2006 label. Tucker also argues that even if a conflict might exist now as a result of the August 2007 class-wide label, no conflict existed in 2002 when GSK could have warned Father Tucker or his physician about Paxil's alleged association with suicidality. Tucker. Br. (Reconsideration) at 1-2.

A motion to reconsider under Federal Rule of Civil Procedure 59 is appropriate where the court has misunderstood a party, where the court has made a decision outside the adversarial issues presented to the court by the parties, where the court has made an error of apprehension (not of reasoning), where a significant change in the law has occurred, or where significant new facts

have been discovered. See *Bank of Waunakee v. Rochester Cheese Sales, Inc.*, 906 F.2d 1185, 1191 (7th Cir. 1990). On reconsideration, the court has re-examined the FDA's regulations concerning drug labeling generally to determine whether those regulations are in actual conflict with state tort law. The court also has taken a second look at Paxil's label to decide whether the FDA's involvement in the warnings to be included on that label in 2007 is in conflict with Tucker's claims that those warnings should have included adult suicidality in 2002.

Undisputed Facts

For purposes of the court's reconsideration of GSK's Motion for Summary Judgment on the issue of preemption, the court incorporates by reference the undisputed facts recounted in its September 19, 2007 Entry. See 2007 WL 2726259, at *1-4. Where necessary, additional undisputed facts are included in the court's discussion, set forth below.

Discussion

I. *Manufacturers' Power and Duty to Revise Warnings*

Under the current version of the FDA's regulations, 21 C.F.R. § 201.80 controls the content and format of labeling for "older" pharmaceuticals, of which Paxil is one. That section provides in part:

> *Warnings.* Under this section heading, the labeling shall describe serious adverse reactions and potential safety hazards, limitations in use imposed by them, and steps that should be taken if they occur. *The labeling shall be revised to include a warning as soon as there is reasonable evidence of an association of a serious hazard with a drug; a causal relationship need not have been proved.*

21 C.F.R. § 201.80(e) (emphasis added).[2] The FDA's regulations also provide the means by which these required revisions should be made, in 21 C.F.R. § 314.70. This provision refers to changes under subsections (b), (c), and (d) as "major," "moderate," and "minor" changes, respectively.

Generally, label changes fall under the category of "major" changes for which prior FDA approval is required. 21 C.F.R. § 314.70(b)(2)(v). The FDA makes an exception for revisions to a drug's label made to add or strengthen a warning. Those changes fall under subsection (c), for "moderate" changes.

[2]Similar language applies to "newer" drugs in 21 C.F.R. § 201.57(c)(6)(i): "In accordance with §§ 314.70 and 601.12 of this chapter, the labeling must be revised to include a warning about a clinically significant hazard as soon as there is reasonable evidence of a causal association with a drug; a causal relationship need not have been definitely established."

21 C.F.R. § 314.70(c)(6)(iii). Most moderate changes require submission of the proposed change to the FDA at least 30 days prior to the distribution of the drug made using the change, and, thus, require a 30-day delay before the change may be implemented. 21 C.F.R. § 314.70(c). But for revisions to a drug's label to add or strengthen a contraindication, warning, precaution, or adverse reaction, the regulations permit a drug manufacturer to make the label change immediately and to distribute the drug under the new label upon submission of a Changes Being Effected ("CBE") supplement to the FDA, without the 30-day waiting period. See 21 C.F.R. §§ 314.70(c)(3), 314.70(c)(6)(iii)(A). If the FDA, after receiving notice of the change, were to disapprove of the change, the FDA could order the manufacturer to cease distribution of the drugs made with the label change. See 21 C.F.R. § 314.70(c)(7). By operation of these regulations, then, drug manufacturers are able to add or strengthen a warning on a drug's label almost immediately upon recognition of a serious hazard. They need wait only as long as it takes to notify the FDA of the change.

GSK has acknowledged that the regulations give it the responsibility for proper labeling of Paxil, and that it had the ability to make changes to Paxil's label when there was "reasonable association" between a serious hazard and a patient's ingestion of the drug. See Tucker Response (Preemption) Ex. 1 (Arning Dep.) at 104-05, Ex. 2 (Agarwal Dep.) at 59-61, 63-65, Ex. 3 (Kline Dep.) at 69-72, 106-08. Nevertheless, GSK argues that "regardless of the form of the supplement, [the]

FDA retains exclusive authority over labeling for prescription drugs." GSK Br. (Preemption) at 10.

This argument fails to appreciate, as the court failed to appreciate, the fact that the ongoing ability, authority, and responsibility to strengthen a label still rest squarely with the drug manufacturer. Although the FDA might later disapprove of a label strengthened pursuant to 21 C.F.R. § 314.70(c) and § 201.80, the FDA's power to disapprove does not make the manufacturer's voluntarily strengthened label a violation of federal law, which is what it would take to establish an actual conflict between state tort law and federal law. The FDA might do nothing, thus giving effect to the change. See 21 C.F.R. § 314.70(c); see also *Witczak v. Pfizer, Inc.*, 377 F. Supp. 2d 726, 729 (D. Minn. 2005). If the FDA exercises its power to disapprove the revised label, the FDA's disapproval is not retroactively illegal; the manufacturer simply stops distributing the new label. See 21 C.F.R. § 314.70(c)(7); *Witczak*, 377 F. Supp. 2d at 729. Thus, prior FDA approval need not be obtained, nor will a product be deemed misbranded,[3] if the manufacturer voluntarily or even unilaterally strengthens the warnings,

[3]The distribution of "misbranded" drugs is prohibited by the FDCA. 21 U.S.C. §§ 331(a), (b). A drug is "misbranded" if its "labeling is false or misleading in any particular," if its labeling lacks "adequate warnings against use . . . where its use might be dangerous to health," or if it is dangerous to health when used in the . . . manner . . . prescribed, recommended, or suggested in the labeling thereof." 21 U.S.C. §§ 352(a), (f), (j). The FDA has the authority to enforce the prohibition on misbranding by initiating injunction proceedings, criminal prosecutions, or seizure of the misbranded drugs. 21 U.S.C. §§ 332, 333(a), 334. The FDA does not have the authority to declare unilaterally that a label is false or misleading and thus that a drug is misbranded; it must proceed to court for a judicial determination in an enforcement action.

precautions or potential adverse reactions listed on a label previously approved by the FDA pursuant to its powers under 21 C.F.R. § 314.70(c) and § 201.80.

Similar regulations governed drug manufacturers at the time of Father Tucker's death. In 2002, 21 C.F.R. § 201.56 described the general requirements for the content and format of drug labeling, and 21 C.F.R. § 201.57 described the specific requirements for the content and format of drug labeling. The language now found in 21 C.F.R. § 201.80(e) was found then in 21 C.F.R. § 201.57(e) (2002) ("The labeling shall be revised to include a warning as soon as there is reasonable evidence of an association of a serious hazard with a drug; a causal relationship need not have been proved."). In 2002, manufacturers also had the power and responsibility to revise a drug's label immediately to reflect reasonable evidence of a drug's association with a serious hazard without waiting for prior FDA approval. See 21 C.F.R. § 314.70 (2002). Paragraph (c)(2) of section 314.70 permitted changes to be made in advance of FDA approval to change a label "to add or strengthen a contraindication, warning, precaution, or adverse reaction." See 21 C.F.R. § 314.70(c)(2)(i)(2002). GSK's relevant obligations, then, were essentially the same in 2002 as they are today.[4]

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[4]This obligation will probably remain in effect in the future. The FDA is in the process of amending 21 C.F.R. § 314.70(c)(6)(iii) to enable drug manufacturers to add or strengthen a warning only upon acquisition of *new* information. Supplemental Applications Proposing Labeling Chances for Approved Drugs, Biologics, and Medical Devices, 73 Fed. Reg. 2848-01, 2849 (proposed Jan. 16, 2008). "Newly acquired" information would include "data, analyses, or other information not previously submitted to the agency, or submitted within a reasonable time period prior to the CBE supplement, that provides novel (continued...)

II. *The FDA's 2006 Preamble on Preemption*

In 2006 the FDA amended its regulations. In the preamble to the amended regulations, the FDA asserted that state failure-to-warn lawsuits, such as the one brought by Tucker here, have "directly threatened the agency's ability to regulate manufacturer dissemination of risk information for prescription drugs." Requirements on Content and Format of Labeling for Human Prescription Drugs and Biological Products, 71 Fed. Reg. 3922, 3934 (Jan. 24, 2006). The FDA asserted that its position was "long standing," and it argued that its labeling requirements are not minimum standards but establish both a "floor and a ceiling." 71 Fed. Reg. at 3934-35. The preamble cautioned that state failure-to-warn lawsuits could "erode and disrupt the careful and truthful representations of the benefits and risks that prescribers need to make appropriate judgments about drug use. Exaggeration of risk could discourage appropriate use of a beneficial drug." *Id*. at 3935.[5] Accordingly, the FDA stated its belief that "claims

[4](...continued)
information about the product, such as a risk that is different in type or severity than previously known risks about the product." *Id*. at 2850. It would not include reports of adverse events that are consistent in type, severity, and frequency with information previously provided to the FDA. *Id*. Also, the FDA proposes to "clarify" that drug manufacturer should use a CBE supplement to strengthen a warning only when there is "sufficient evidence of a causal association," consistent with the requirements of 21 C.F.R. § 201.57(c) ("reasonable evidence of a causal association; a causal relationship need not have been definitely established."). *Id*. at 2850-51. Even with these proposed amendments, which the FDA does not consider to be "substantive" changes, *id*. at 2851, the obligation to add to or strengthen a warning on a drug's label will rest with the manufacturer immediately upon discovery of new information giving rise to "reasonable evidence of a causal association" between the drug and the hazard.

[5]The FDA has echoed this opinion in *amicus* briefs filed in other courts. For (continued...)

that a sponsor breached an obligation to warn by failing to include contraindications or warnings that are not supported by evidence that meets the standards set forth in this rule" are preempted. *Id.* at 3935-36. The FDA conceded, however, that failure-to-warn claims based on state-law duties that parallel federal ones, or that seek to enforce federal duties, are not preempted. *Id.* at 3936; see also *Medtronic, Inc. v. Lohr*, 518 U.S. 470, 496-97 (1996) (holding that tort claim premised on state-law duties "equal to, or substantially identical to" duties imposed by federal law is not preempted).

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[5](...continued)
example, it submitted the following opinion regarding preemption in a similar case before the Eastern District court of Pennsylvania:

> It is critical to understand that, where warnings are concerned, more is not always better. In setting standards for drug labeling, [the] FDA seeks to encourage the optimal level of use in light of reasonable safety concerns, by requiring scientific evidence that establishes an association between a drug and a particular hazard before warning of that association on a drug's labeling. Under-use of a drug based on dissemination of the unsubstantiated warnings may deprive patients of efficacious and possibly life-saving treatment. Further, allowing unsubstantiated warnings would likely diminish the impact of valid warnings by creating an unnecessary distraction and making even valid warnings less credible.

GSK Reply (Preemption) Ex. 2 at 16-17 (Brief of *Amicus Curiae* United States of America, *Colacicco v. Apotex, Inc.*, 432 F. Supp.2d 514 (E.D. Pa. 2006) (dismissing plaintiff's failure-to-warn claim against GSK on conflict preemption grounds), affirmed, 521 F.3d 253 (3rd Cir. 2008)). The FDA reaffirmed this position earlier this year in its proposed amendments to § 314.70: "Exaggeration of risk, or inclusion of speculative or hypothetical risks, could discourage appropriate use of a beneficial drug . . . . As [the] FDA has stated, labeling that includes theoretical hazards not well-grounded in scientific evidence can cause meaningful risk information to lose its significance." 73 Fed. Reg. at 2851.

Although "a specific expression of agency intent to pre-empt, made after notice-and-comment rulemaking" is not necessary to find conflict preemption, see *Geier v. American Honda Motor Co.*, 529 U.S. 861, 885 (2000), in another area where the FDA has claimed that its regulatory action preempts state law – medical devices – it has said so explicitly in regulations adopted through notice and comment proceedings having the force of law, pursuant to Congress' clear expression of preemption. See, *e.g.*, 21 U.S.C. § 360k(a) (Medical Device Amendments of 1976); 21 C.F.R. § 808.1; see also *Riegel v. Medtronic, Inc.*, 552 U.S. —, 128 S. Ct. 999 (2008) (considering the effect of the express preemption provision of the MDA and holding that tort claims for medical device were preempted). Not so here. Here, the FDA has staked a claim for preemption only in the preamble to the regulations and in legal briefs submitted in litigation against drug manufacturers.

Regulations promulgated according to federal statutory authority "have no less pre-emptive effect than federal statutes." *Fidelity Federal Savings and Loan Ass'n v. de la Cuesta,* 458 U.S. 141, 153 (1982). The FDA is authorized to promulgate regulations that have the preemptive force of law, so long as the regulations are properly adopted and in accord with statutory authority. *E.g.*, *City of New York v. F.C.C.*, 486 U.S. 57, 63-64 (1988). Ordinarily, an agency's interpretation of its own regulation is entitled to great deference where either the statute or the regulation is ambiguous. See generally *Chevron U.S.A., Inc. v. Natural Resources Defense Council, Inc.*, 467 U.S. 837 (1984). *Chevron* deference

is warranted, however, only when the agency speaks in the exercise of its authority "to make rules carrying the force of law." *United States v. Mead Corp.*, 533 U.S. 218, 226-27 (2001).

In *Geier v. Honda*, the Supreme Court addressed the weight to be given to an agency's position on preemption. The Court "place[d] some weight" on the agency's interpretation, put forth in an *amicus* brief, of the preemptive effect of a rule it had promulgated. See 529 U.S. at 883. The Court's discussion in *Geier* shows that the FDA's opinion regarding preemption may be considered even though it is not in a formal regulation and that the FDA's opinion is subject to a level of deference approximating that set forth in *Skidmore v. Swift & Co.*, 323 U.S. 134, 139-40 (1944) (agency policies, made in pursuit of official duty and based on specialized experience and broad investigation and information, but not reached as a result of hearing adversary proceedings with findings of fact and conclusions of law, are not binding but are entitled to respect); see also *United States v. Mead Corp.*, 533 U.S. 218 (2001) (giving *Skidmore* deference to a tariff classification ruling by the federal customs service upon finding no indication that Congress intended such a ruling to carry the force of law). As the Court has stated, "agencies may play the sorcerer's apprentice but not the sorcerer himself." *Alexander v. Sandoval*, 532 U.S. 275, 291 (2001).

In the 2006 preamble opinion on preemption, the FDA was not interpreting either the FDCA or one of its regulations. It was instead attempting to "supply,

on Congress' behalf, the clear legislative statement of intent required to overcome the presumption against preemption." *Desiano v. Warner-Lambert & Co.*, 467 F.3d 85, 97 n.9 (2d Cir. 2006) (dictum). The FDA's construction is entitled to respect only to the extent of its "power to persuade." *Mead*, 533 U.S. at 228, quoting *Skidmore*, 323 U.S. at 140. Accordingly, the FDA's pronouncements are not controlling, but the court recognizes that the FDA's opinions originate from "a body of experience and informed judgment to which courts and litigants may properly resort for guidance." *Skidmore*, 323 U.S. at 140. The weight a court should give an agency opinion in a particular case will depend on "the thoroughness evident in its consideration, the validity of its reasoning, its consistency with earlier and later pronouncements, and all those factors which give it power to persuade, if lacking power to control." *Skidmore*, 323 U.S. at 140; see also *Mead Corp.*, 533 U.S. at 228 (considering "the degree of the agency's care, its consistency, formality, and relative expertness, and . . . the persuasiveness of the agency's position" in weighing agency's opinion).

The FDA's current position on preemption is not "long standing" but is in fact a "180-degree reversal" from its earlier stance. David A. Kessler & David C. Vladeck, *A Critical Examination of the FDA's Efforts to Preempt Failure-to-Warn Claims*, 96 Geo. L.J. 461, 474 n.59 (2008). In 1979, the FDA declared, "it is not the intent of the FDA to influence civil tort liability of the manufacturer." Labeling and Prescription Drug Advertising; Content and Format for Labeling for Human Prescription Drugs, 44 Fed. Reg. 37,434, 37,477 (June 26, 1979). More recently,

in 1994, the FDA recognized "the sophistication and complexity of private tort litigation in the United States and the proposed preemption action is not intended to frustrate or impede tort litigation in this area. Indeed, [the] FDA recognizes that product liability plays an important role in consumer protection." Protecting the Identities of Reporters of Adverse Events and Patients; Preemption of Disclosure Rules, 59 Fed. Reg. 3944, 3948 (proposed Jan. 27, 1994). Four years later, the FDA stated that its guidelines established the minimum labeling standards but that states could authorize additional labeling. Prescription Drug Product Labeling; Medication Guide Requirements, 63 Fed. Reg. 66,378, 66,384 (Dec. 1, 1998) ("[The] FDA's regulations establish the minimal standards necessary, but were not intended to preclude the states from imposing additional labeling requirements. States may authorize additional labeling, but they cannot reduce, alter, or eliminate FDA-required labeling."). And, as recently as 2000, the FDA disavowed any "federalism implications" or preemptive effect of changes to its requirements for prescription drug labeling. Requirements on Content and Format of Labeling for Human Prescription Drugs and Biologics; Requirements for Prescription Drug Product Labels, 65 Fed. Reg. 81,082, 81,103 (proposed Dec. 22, 2000). These shifts do not show that the FDA's current position is necessarily wrong, but they demonstrate that the FDA's current view on the preemptive effect of its regulations deserves less deference than a more consistent view might.

The remaining *Skidmore* factors also weigh against giving the FDA's opinion on preemption much deference. The FDA has not engaged in notice-and-comment

rulemaking on this issue. While those procedures are not required under *Geier*, the lack of process decreases the level of formality and weight of the FDA's opinion. Also, while the FDA has a great deal of expertise in regulating the pharmaceutical industry, this expertise does not extend to what is ultimately a question of federal law and congressional policy. The expertise needed here may be found in Congress and in the federal and state courts, not necessarily in regulatory agencies. Accordingly, the court, on reconsideration, gives relatively little weight to the FDA's opinion on the preemptive effect of its regulations.

III. *Balance Between FDA Regulations and Failure-to-Warn Claims*

To demonstrate that an actual conflict exists between the FDA's regulations and state tort law, GSK must demonstrate either that it is impossible for it to comply with both state and federal requirements, or that state tort law stands as an obstacle to the accomplishment and execution of the full purposes of the FDA regulations as an expression of Congress' objectives under the FDCA. See *Sprietsma*, 537 U.S. at 64.

The conflict that GSK raises is that drug manufacturers will be forced to walk a tightrope between being sanctioned by the FDA for "overwarning" and being sanctioned by the courts for "underwarning." In other words, GSK sees a world in which it must choose between either avoiding tort liability by revising a drug's labeling to warn against non-existent risks, thus "misbranding" the drug under the FDCA and the FDA's regulations, or adhering to the FDA's requirements for labeling and risking tort liability for failing to provide a warning against a hazard that has no reasonable causal relationship to the drug. GSK Br. (Preemption) at 4, 8. GSK has not provided any examples of the FDA punishing it or any other drug manufacturer for overwarning.[6] Nor has GSK provided a specific example of a runaway jury verdict in which a jury found for a plaintiff in a failure-to-warn

[6]In 2004, the FDA required Wyeth Pharmaceuticals to add additional language to a strengthened warning in a "Changes Being Effected" supplement. GSK Reply (Preemption) Ex. 4. However, requiring clarification to warning language is not a sanction for the issuance of a strengthened warning and does not establish a conflict for preemption purposes.

case, in which the warning sought had been deemed "unsubstantiated" by the FDA, and the verdict survived appellate review.

As the regulations stand, drug manufacturers have the authority to strengthen warnings without the advance permission of the FDA. The current version of the regulations permits manufacturers to act unilaterally to add and strengthen warnings, subject to subsequent FDA approval. All that is necessary to trigger a drug manufacturer's obligation to strengthen the warnings on a drug's label regarding serious hazards is "reasonable evidence of an association of a serious hazard with a drug." 21 C.F.R. § 201.80(e).

By comparison, a plaintiff bringing a failure-to-warn claim must demonstrate that the drug caused the harm the plaintiff suffered and that the manufacturer failed to provide an appropriate warning against that harm. See, *e.g.*, Ind. Code § 34-20-4-2 ("A product is defective under this article if the seller fails to: (1) properly package or label the product to give reasonable warnings of danger about the product . . . "). As with any fault-based action, causation is an essential element of a failure-to-warn claim and must be proved to the fact finder by a preponderance of the evidence. GSK argues that drug manufacturers will be forced to place scientifically unsubstantiated warnings on their drug products unless state law tort claims are preempted. GSK Br. (Preemption) at 4, 22; GSK Reply (Preemption) at 7. However, when functioning properly, tort law should

guard against this risk by forcing plaintiffs to carry their burden of proving causation.[7]

The court recognizes, of course, that tort litigation is far from infallible in evaluating evidence of risks associated with drugs. But the FDA's regulatory process also is not infallible. Recognizing that neither process is infallible, there is no inherent conflict here. In this framework, which is consistent with existing statutes and regulations, failure-to-warn litigation can serve to reinforce the FDA's regulations, which already place the obligation to strengthen the warnings on a drug's label squarely on the shoulders of the drug's manufacturer. The source of the "reasonable evidence of a causal association" triggering this obligation could be the drug manufacturer's research, it could be research received and reviewed by the FDA, or, consistent with the goals and objectives of the FDCA, it could come to light as a result of a failure-to-warn lawsuit. It is worth recalling here that under the defendant's preemption theory here, a plaintiff could not recover for an injury or death even if the plaintiff could prove beyond reasonable dispute: (a) that the manufacturer failed to provide a warning of a significant and genuine hazard (not recognized by the FDA), (b) that the failure proximately caused serious harm or even death, and thus indirectly (c) that the FDA regulatory process had failed to identify a significant danger.

[7]Under Indiana law, GSK would enjoy a rebuttable presumption that Paxil's warnings were adequate if it can show that it was in compliance with the FDA's regulations. See Ind. Code § 34-20-5-1(2) (in product liability action, there is a rebuttable presumption that the manufacturer was not negligent if before the sale, the product complied with applicable federal or state regulations).

The FDA does not conduct its own drug trials and "does not have sufficient authority to require additional clinical trials after drug approval." Mary J. Davis, *The Battle Over Implied Preemption: Products Liability and the FDA*, 48 B.C. L. Rev. 1089, 1149 (2007). "To place the postmarket obligation exclusively on the FDA and other public groups would destroy the ability of the FDA to regulate effectively the postmarketing risks stemming from the large number of prescription drugs it oversees." *Id*. As one former FDA Administrator summed up the regulatory situation:

> The most fundamental problem is that drugs are approved on the basis of clinical testing that cannot, and is not designed to, uncover risks that are relatively rare or have long latency periods. Legislation cannot solve this problem. . . . Top-down surveillance is no substitute for failure to warn litigation, which provides the FDA, doctors, and patients with information about new risks that is otherwise unavailable to the agency.

Kessler & Vladek, *supra*, at 483-84.

Tort law can play an important role in filling the gap, and it is consistent with a regulatory system that puts the obligation to warn on the party with the most comprehensive information available: the drug manufacturer. The possibility that a jury might find in favor of a plaintiff advocating an unsubstantiated warning is an insufficient basis for finding that *all* pharmaceutical failure-to-warn claims should be preempted and that *all* failure-to-warn plaintiffs should be denied any legal recourse if their theories conflict with current FDA positions. Plaintiffs in such cases – and this looks like one of them

– face a steep hill to meet their burden of proof. But if they can meet that burden, the court will need to listen.

IV. *No Actual Conflict in This Case, Yet*

GSK argues that an actual conflict exists under the specific facts of this case. GSK asserts that the FDA repeatedly considered and rejected the precise warning that Tucker advocates. GSK Br. (Preemption) at 1-3, 29; see also GSK Reply (Preemption) at 2 ("Plaintiff's state-based tort claims are all grounded on the alleged failure to provide a warning that would have violated federal law. Therein lies the conflict. It is so stark a more obvious one is difficult to envision."), 3, 8, 17. In the original Entry, the court found these arguments persuasive.

In particular, the court was swayed by the fact that, in May 2006, GSK revised Paxil's label to include the following warning:

> In adults with [major depressive disorder] (all ages), there was a statistically significant increase in the frequency of suicidal behavior in patients treated with [Paxil] compared with placebo (11/3,455 [0.32%] versus 1/1,978 [0.05%]); all of the events were suicide attempts. However, the majority of these attempts for [Paxil] (8 of 11) were in younger adults aged 18-30 years. These MDD data suggest that the higher frequency observed in the younger adult population across psychiatric disorders may extend beyond the age of 24.

2007 WL 2726259, at *4, citing Docket No. 150, Ex. 2 at 12. In the meantime, the FDA engaged in its own evaluation of whether all antidepressants, as a class of drugs, were associated with an increased risk of suicidality in adults. Based on recommendations from the Psycho-pharmacological Drugs Advisory Committee,

the FDA contacted GSK in May 2007 and required GSK to revise the label for Paxil to include a class-wide warning that included the following language: "Short term studies did not show an increase in the risk of suicidality with antidepressants compared to placebo in adults beyond age 24." See 2007 WL 2726259, at *4, citing Dkt. No. 149, Ex. C. The court found that this FDA-mandated warning "confirms the risk of suicidality in pediatric patients, but affirmatively rejects the hypothesis that there is any such association in adults," and that this revised labeling "stands in clear and undeniable conflict with Tucker's state law causes of action." *Id*. at *9.

On reconsideration, the court finds this position flawed in one key respect: in spite of the FDA's direction regarding Paxil's label in May 2007, GSK still had (and has) the obligation to revise its label to strengthen a warning upon reasonable evidence of an association of a serious hazard, particularly with respect to this individual drug. If GSK were to receive such evidence, it would be obligated to revise its label in spite of the FDA's directive in May 2007. In fact, when it issued its instruction that GSK revise Paxil's label, the FDA advised GSK that if GSK disagreed with the FDA's belief that Paxil-specific analysis should be included in the SSRI labeling revisions, GSK could request a meeting with the FDA. Tucker Br. (Reconsideration) Ex. 1. The FDA's offer, upon which GSK did not act, is consistent with GSK's ongoing obligations under the regulations. In other words, the FDA's revisions were not necessarily the final word on Paxil's

label and did not put GSK into a position where it was impossible for GSK to comply with both state and federal law.

Moreover, to preempt Tucker's claims based on actions by the FDA in 2007 would have the effect of retroactively absolving GSK of a duty it might have owed to Father Tucker in the fall of 2002. Regardless of what the FDA ordered in 2007, if GSK had evidence of a reasonable association between Paxil and adult suicidality in 2002, it had the duty then under the FDA's regulations to strengthen the warnings on Paxil's label. GSK had no way of knowing in 2002 what the FDA would order in 2007. The possibility that the FDA might come to a different scientific conclusion in the future regarding a drug's associated risks does not erase the drug company's present and ongoing obligation to take immediate action to warn the public of the association with a serious hazard. What the FDA ordered in 2007, and its scientific basis for doing so, will no doubt be relevant as to whether the available evidence was sufficient to trigger GSK's obligation to issue an adult suicidality warning in 2002. But the FDA's later decision does not create an actual conflict such that Tucker's claims arising in 2002 should be preempted.[8]

[8]The court considered and rejected a similar but not identical argument in its September 19, 2007 Entry, finding that "Tucker has not shown how the language currently required by the FDA would have been heeded any differently than the similar language that actually accompanied the drug when Father Tucker was taking it." 2007 WL 2726259, at *10. This point cuts towards what Tucker's burden will be to show causation, not towards whether GSK would be unable to comply with both state tort and federal regulatory requirements, which is the issue presented here.

To be sure, the FDA stated in an *amicus* brief filed in another court in 2006 that, as of October 2003, it had determined that adult suicidality warnings on Paxil's label would have been "false and misleading." See GSK Reply (Preemption) Ex. 2 at 16; see also GSK Br. (Preemption) at 3, 10 ("[h]ere, regardless of whether GSK had submitted either type of supplement – which it could not do in the absence of a scientifically valid basis – the warning about suicidality that Plaintiff claims should have been given by GSK prior to August 2002, would not have been approved. FDA has said so."). The FDA's statement, made outside of these proceedings is, at most, evidence regarding whether or not GSK was faced with reasonable evidence of an association between Paxil and adult suicidality in the fall of 2002 sufficient to trigger its duty to warn. The FDA's statement, again, would not have retroactively dissolved GSK's 2002 duty to revise its label in the face of the appropriate level of evidence of adult suicidality, if it in fact had such evidence. The FDA's statement, made several years after the fact, that it would not have approved a warning change that was never actually proposed, is speculative and will not serve as the basis for a finding of a preemptive conflict.

Finally, GSK argues that if it had implemented the warnings Tucker advocates, it would have risked prosecution for distributing a misbranded drug, and thus was in an impossible position, sufficient to demonstrate actual conflict. GSK Br. (Preemption) at 1-2, 4, 8; GSK Reply (Preemption) at 2, 7, 9. This argument presumes that GSK was not in possession of evidence of a reasonable association between Paxil and adult suicidality at any time prior to the FDA's

implementation of the class-wide label in 2007, because, of course, such evidence would have obligated GSK to revise its label regardless of what the FDA would eventually come to believe. This is reflected by the fact that in May 2006, GSK unilaterally changed Paxil's label to reflect a stronger warning regarding adult suicidality, without any retribution by the FDA. The FDA did not reject the strengthened warning and did not prosecute GSK for distributing a "misbranded" drug. True, a year later the FDA decided that a class-wide antidepressant label was more appropriate for Paxil. In the face of that directive, if GSK were to continue to distribute Paxil under a Paxil-specific label, it would indeed risk FDA enforcement actions under 21 U.S.C. §§ 332, 333, 334(a), or 337(a). And if GSK were forced into a position where it had to choose between compliance with the FDA's directives or avoiding tort liability, it would be placed in an actual conflict sufficient to find preemption.

However, that is not the case here, at least not yet. Again, GSK's argument that it might face prosecution for strengthening its label assumes that no new evidence will ever come to light establishing a reasonable association between Paxil and adult suicidality or any other serious hazard. Such evidence, if it did come to light, would immediately trigger GSK's responsibility under the regulations to revise Paxil's label, regardless of what the FDA had to say about the appropriateness of class-wide labeling in 2007. GSK's possible future risk of prosecution for distribution of a misbranded drug would present a conflict only if GSK could state with absolute certainty that it will never have new evidence

sufficient to trigger its obligations under the regulations to revise its label to strengthen a warning with Paxil-specific language, but is forced to do so by state tort law.[9] This position is not only speculative, but, as discussed above, failure-to-warn claims should require a much stronger showing of causation than the regulations do. Rather than forcing GSK to choose between overwarning or underwarning, failure-to-warn claims fit into this framework and will not impose any additional obligations on GSK that are not already imposed by the regulations. The FDA's 2007 directive regarding Paxil's label did not alter GSK's duties or obligations under the regulations, and it is not impossible for GSK to comply with those regulations and its duties in tort. Therefore, the court finds that Tucker's state law tort claims are not preempted under federal law.

Conclusion

Because the court finds that Tucker's claims are not preempted, Tucker's claims against GSK are reopened for adjudication on the merits. The judgment entered on September 19, 2007 is hereby VACATED. GSK's motion for summary

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[9]This position is consistent with the FDA's opinion regarding the preemptive impact of its proposed amendment to §314.70(c):

> To the extent that state law would require a sponsor to add information to the labeling for an approved drug . . . without advance FDA approval based on information or data as to risks that are similar in type or severity to those previously submitted to the FDA, or based on information or data that does not provide sufficient evidence of a causal association with the product, such a state requirement would conflict with federal law.

73 Fed. Reg. at 2853.

judgment on the issues of causation and breach of duty is no longer moot. The court will address the merits of GSK's motion in the near future, based on the papers previously submitted by the parties, to see if plaintiff Tucker can actually meet the high standard of causation needed here.

So ordered.

Date: July 18, 2008

DAVID F. HAMILTON, CHIEF JUDGE
United States District Court
Southern District of Indiana

Copies to:

Andrew T. Bayman
KING & SPALDING LLP
abayman@kslaw.com

Mark S. Brown
KING & SPALDING LLP
mbrown@kslaw.com

L. Frank Coan , Jr
KING & SPALDING LLP
fcoan@kslaw.com

Todd P. Davis
KING & SPALDING LLP
tdavis@kslaw.com

Bijan Esfandiari
BAUM HEDLUND ARISTEI & GOLDMAN, P.C.
besfandiari@baumhedlundlaw.com,gbrown@baumhedlundlaw.com

Bonnie L. Gallivan
ICE MILLER LLP
gallivan@icemiller.com,ramona.king@icemiller.com

Robert E. Glanville
PHILLIPS LYTLE LLP
rglanville@phillipslytle.com

Ronald L.M. Goldman
BAUM HEDLUND ARISTEI & GOLDMAN P.C.
rgoldman@baumhedlundlaw.com,mcornwell@baumhedlundlaw.com

Tamar P. Halpern
PHILLIPS LYTLE LLP
thalpern@plllp.com

George W. Murgatroyd , III
BAUM HEDLUND ARISTEI & GOLDMAN PC
gmurgatroyd@baumhedlundlaw.com,chall@baumhedlundlaw.com

David F. Norden
KING & SPALDING LLP
dnorden@kslaw.com

Frances M. Phares
BAUM HEDLUND ARISTEI & GOLDMAN, P.C.
fphares@baumhedlundlaw.com,sbeam@baumhedlundlaw.com

Chilton Davis Varner
KING & SPALDING LLP
cvarner@kslaw.com,ayeary@kslaw.com

Dylan A. Vigh
DULIK & VIGH
dvighlaw@gmail.com

Katherine A. Winchester
ICE MILLER LLP
winchest@icemiller.com,ramona.king@icemiller.com